(b) [a partial sequence at least 14 base pairs in length of the sequence defined under (a),

(c)] a sequence hybridizing with any of the sequences defined under (a) in 2 x SSC at 60°C,

[(d) a sequence exhibiting at least 70% identity with any of the sequences defined under (a) between position 1295 and position 2195 from SEQ ID NO: 1, or between position 432 and position 1318 from SEQ ID NO: 3, or between position 154 and position 1123 from SEQ ID NO: 5,

(e)] (c) a sequence complementary to the sequences defined under (a), and

[(f)] (d) a sequence which, due to degeneracy of the genetic code, encodes the same amino acid sequences as those encoded by the sequences defined under (a), [(b), (c) and (d)]

wherein said nucleic acid encodes a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells.

22. (Twice Amended) The nucleic acid of Claim 1(b) [(c)] which comprises a sequence that hybridizes with a sequence defined under (a) in 0.5 x SSC at 60°C.

23. (Twice Amended) The nucleic acid of Claim 1(b) [(c)] which comprises the sequence that hybridizes with a sequence defined in (a) in 0.2 x SSC at 60°C.

REMARKS

The Official Action dated November 8, 2000, has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present Application in condition for allowance. Reconsideration is respectfully requested.

Claims 8-9, 11-20, and 32-33 have been canceled. Claims 1 and 22-23 have been amended. Support for the amendment to Claim 1 can be found in the specification as originally filed on page 4, lines 10-11 and page 5, lines 1-3. Claims 22-23 have been amended as to form.

As the amendments to the claims are supported by the specification as filed and add no new matter, entry is believed to be in order and is respectfully requested.

Claims 1-7, 10, 17 and 22-31 have been rejected under 35 U.S.C. § 112, first paragraph, as not being supported by an enabling specification. The Examiner alleges that the specification does not reasonably provide enablement for any and all partial sequences which are at least 14 base pairs in length of the sequences according to SEQ ID NOS:1, 3 or 5, or any and all sequences which exhibit at least 70% identity between position 1295 and position 2195 from SEQ ID NO: 1, or between position 432 and position 1318 from SEQ ID NO: 3, or between position 154 and position 1123 from SEQ ID NO: 5. The Examiner further alleges that the specification fails to teach which of the claimed nucleic acids encode a polypeptide which can be used as intended, i.e. to screen for pesticides, and that the Applicants have failed to show how to determine which of the claimed nucleic acids can be used as intended.

As will be set forth below, Applicants submit that Claim 1, and Claims 2-7, 10 and 22-31 dependent directly or indirectly, thereon are supported by an enabling specification. Accordingly, the rejection is traversed and reconsideration is respectfully requested.

Claim 1, as amended, recites an isolated nucleic acid comprising a sequence selected from:

(a) a sequence according to nucleotide No. 372 to nucleotide No. 2681 of SEQ ID NO: 1, nucleotide No. 335 to nucleotide No. 1822 of SEQ ID NO: 3 and nucleotide No. 95 to nucleotide No. 1597 of SEQ ID NO: 5,

(b) a sequence hybridizing with any of the sequences defined under (a) in 2 x SSC at 60°C,

(c) a sequence complementary to the sequences defined under (a), and

(d) a sequence which, due to degeneracy of the genetic code, encodes the same amino acid sequences as those encoded by the sequences defined under (a),

wherein said nucleic acid encodes a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells. Claim 1 no longer recites a partial sequence at least 14 base pairs in length of the sequence defined under (a) or a sequence exhibiting at least 70% identity with any of the sequences defined under (a) between position 1295 and position 2195 from SEQ ID NO: 1, between position 432 and position 1318 from SEQ ID NO: 3, or between position 154 and position 1123 from SEQ ID NO: 5.

Nucleic acids which encode a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells, as recited in Claim 1, encode a polypeptide which can be used to screen for insecticidal substances. The specification teaches that the nucleic acids according to the invention may be used to discover insecticidal substances by introducing a recombinant DNA molecule encompassing at least one nucleic acid in accordance with the invention into a host cell, culturing the host cell under conditions which permit expression of the receptors and in the presence of a compound to be tested, and detecting any change in receptor properties (page 6, line 28-page 7, line 6).

A suitable culturing method and method for detecting changes in receptor properties are set forth on page 14, line 25-page 15, line 26. Briefly, the host cells may be cultured in Dulbecco's modified Eagle's medium supplemented with fetal calf serum and Zeocin. As acetylcholine receptors are ligand-regulated ion channels, changes in receptor properties may be determined by detecting alterations in intracellular calcium concentration by treating the host cells in the presence of the compound to be tested with Fura-2-acetoxy methyl ester, and determining fluorescence intensity before and after treatment with a ligand (nicotine). Thus the specification teach one of ordinary skill how to determine whether nucleic acids can be used as intended, namely, how to use the nucleic acids to determine whether compounds modulate the conducting properties of acetylcholine receptors.

Therefore, for the reasons set forth above, Claim 1, and Claims 2-7, 10 and 22-31 dependent directly or indirectly, are supported by an enabling specification, whereby the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Claims 1-7, 10, 17 and 22-31 have been rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner alleges that Claims 1-7, 10, 17 and 22-31 are indefinite as it is unclear what is intended by "partial acetylcholine receptor". The Examiner alleges that Claim 17 is further indefinite because it recites "[t]he regulatory sequence of claim 3" and "the nucleic acid" without proper antecedent basis, and because it is unclear which regulatory sequence and which amino acid is intended.

As will be set forth below, Applicants submit that Claim 1, and Claims 2-7, 10 and 22-31 dependent directly or indirectly thereon, are definite. Accordingly, the rejection is traversed and reconsideration is respectfully requested.

The Examiner alleges that it is unclear what is intended by "partial acetylcholine receptor". Claim 1, as amended, recites an isolated nucleic acid which encodes a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells. Applicants submit that one of ordinary skill will appreciate that a "partial acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells" refers to a protein comprising fewer amino acids that the complete native protein but which still exhibits an ability to form homoligomeric receptors. Thus, Claim 1 and Claims 2-7, 10 and 22-31 dependent thereon are definite, whereby the rejection of Claims 1-7, 10 and 22-31 should be reversed.

Claim 17 has been canceled, whereby the rejection as to Claim 17 has been overcome.

For the reasons set forth above, Claims 1-7, 10 and 22-31 are definite, whereby the rejection under 35 U.S.C. § 112, second paragraph, should be reversed.

Claim 1 has been rejected under 35 U.S.C. § 102 as being anticipated by Schulte et al. The Examiner alleges that Schulte et al. teach GenBank Accession No. AF143486, which is 97.8% identical to SEQ ID NO:1 and 100% identical to SEQ ID NO:3 between positions 432 and 1318, and GenBank Accession No. AF143487, which is 97.34% identical to SEQ ID NO:5 and 100% identical to SEQ ID NO:5 between positions 154 and 1123.

As will be set forth below, Applicants submit Schulte et al. is not a proper reference. Accordingly, the rejection is traversed and reconsideration is respectfully requested.

A certified translation of the priority document, German Application 19819829.9, was filed October 27, 2000, whereby Applicants have perfected a claim for the priority date of May 4, 1998. Thus Schulte et al., published by deposition in GenBank on April 19, 1999, is not a proper § 102 reference, whereby the rejection of Claim 1 under 35 U.S.C. § 102 based on Schulte et al. is overcome.

Claim 1 has been rejected under 35 U.S.C. § 102 as being anticipated by Celniker et al., Liao et al., or Vogel. The Examiner alleges that Celniker et al. teach GenBank Accession No. AC004326, which is 99.4% identical to bases 9-836 of SEQ ID NO:1 and which contains 340 bases identical to bases 496 to 836 of SEQ ID NO:1. Further, the Examiner alleges that Liao et al. teach GenBank Accession No. AF045432 which is identical to SEQ ID NO: 3 over a length of 79 bases, and that Vogel et al. teach GenBank Accession No. Z97178 which is identical to SEQ ID NO: 5 over a length of 98 bases.

As will be set forth below, Applicants submit that Claim 1 is not anticipated by Celniker et al., Liao et al., or Vogel et al. Accordingly, the rejection is traversed and reconsideration is respectfully requested.

As discussed above, Claim 1 recites an isolated nucleic acid comprising a sequence selected from:

(a) a sequence according to nucleotide No. 372 to nucleotide No. 2681 of SEQ ID NO: 1, nucleotide No. 335 to nucleotide No. 1822 of SEQ ID NO: 3 and nucleotide No. 95 to nucleotide No. 1597 of SEQ ID NO: 5,

(b) a sequence hybridizing with any of the sequences defined under (a) in 2 x SSC at 60°C,

(c) a sequence complementary to the sequences defined under (a), and

(d) a sequence which, due to degeneracy of the genetic code, encodes the same amino acid sequences as those encoded by the sequences defined under (a).

Claim 1 requires that the nucleic acid encodes a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells.

Anticipation requires that every element of the claimed invention be disclosed in the prior art reference. *Akzo N.V. v. The United States International Trade Commission*, 808 F.2d 1471, 1479 (Fed. Cir. 1986), cert. denied, 482 U.S. 909 (1987). Celniker et al. teach the sequence of an alcohol dehydrogenase reagion of Drosophila melanogaster DNA, Liao et al. teach the sequence of a zebrafish stem cell leukemia protein (tal-1) mRNA and teaches that a SCL/tal-1 transcription factor acts downstream of cloche to specifically hematopoietic and vascular progenitors, while Vogel et al. teach the sequence of a Beta vulgaris (beet) cDNA for elongation factor 2. None of the cited references disclose a nucleic acid which encodes a complete or partial insect acetylcholine receptor subunit having the ability to form homooligomeric acetylcholine receptors when expressed in host cells, thus none of the references disclose every element of Claim 1.

Further, the Examiner alleges that Celniker et al. teach a sequence which is 99.4% identical to bases 9-836 of SEQ ID NO: 1 and which contains 340 bases identical to bases 496 to 836 of SEQ ID NO: 1. In contrast, Claim 1 recites a sequence according to nucleotide No. 372 to nucleotide No. 2681 of SEQ ID NO: 1, and sequences hybridizing to that sequence, complementary to that sequence, and encoding the same amino acid as that sequence. The 828 and 340 base sequences of Celniker et al. do not teach or suggest the 2310 base pair sequence of SEQ ID NO: 1 recited in Claim 1.

The Examiner alleges that Liao et al. teach a sequence which is identical to SEQ ID NO:3 over a length of 79 bases. In contrast, Claim 1 recites a sequence according to nucleotide No. 335 to nucleotide No. 1822 of SEQ ID NO: 3, and sequences hybridizing to that sequence, complementary to that sequence, and encoding the same amino acid as that sequence. The 79 base sequence of Liao et al. does not teach or suggest the 1487 base pair sequence of SEQ ID NO: 3 recited in Claim 1.

Vogel et al. teach GenBank Accession No. Z97178 which is identical to SEQ ID NO: 5 over a length of 98 bases. In contrast, Claim 1 recites a sequence

according to nucleotide No. 95 to nucleotide No. 1597 of SEQ ID NO: 5, and sequences hybridizing to that sequence, complementary to that sequence, and encoding the same amino acid as that sequence. The 98 base sequence of Vogel et al. does not teach or suggest the 1502 base pair sequence of SEQ ID NO:3 recited in Claim 1.

For the reasons set forth above, Claim 1 is not anticipated by the cited references, whereby the rejection of Claim 1 under 35 U.S.C. § 102 based on Celniker et al., Liao et al., or Vogel.

Claim 2-7 and 24-31 have been rejected under 35 U.S.C. § 103 as being unpatentable over any one of Schulte et al., Celniker et al., Liao et al., or Vogel et al. in view of Ausubel et al. The Examiner relies on Schulte et al., Celniker et al., Liao et al., and Vogel et al. as teaching the sequences discussed above. The Examiner alleges that Ausubel et al. teaches the introduction of nucleic acids into host cells and the use of vectors to do so.

As discussed above, Schulte et al. is not a proper reference, whereby the rejection based on Schulte et al. in view of Ausubel et al. is overcome.

As will be set forth below, Applicants submit that Claim 2-7 and 24-31 are not rendered obvious by any one of Celniker et al., Liao et al., or Vogel et al. in view of Ausubel et al. Accordingly, the rejection is traversed and reconsideration is respectfully requested.

The deficiencies of the primary references with respect to Claim 1, on which Claims 2-7 and 24-31 depend, have been set forth above. Ausubel et al. broadly disclose methods of introduction of DNA into mammalian cells, such as calcium phosphate transfection, DEAE-dextran transfection, electroporation, and lipsome-mediated transfection. The addition of Ausubel et al. will not overcome the deficiencies of the primary references.

As discussed above, the 828 and 340 base sequences of Celniker et al. do not teach or suggest the 2310 base pair sequence of SEQ ID NO:1 recited in Claim 1, the 79 base sequence of Liao et al. does not teach or suggest the 1487 base pair sequence of SEQ ID NO:3 recited in Claim 1, and the 98 base sequence of Vogel et al. does not teach or suggest the 1502 base pair sequence of SEQ ID NO:3 recited in Claim 1. Applicants find no teaching or suggestion in Ausubel et al. of the 2310

base pair sequence of SEQ ID NO:1, the 1487 base pair sequence of SEQ ID NO:3, the 1502 base pair sequence of SEQ ID NO:3 recited in Claim 1, or of sequences hybridizing to those sequences, complementary to those sequences, or encoding the same amino acid as those sequences. Thus, none of the references, individually or combined, suggest the sequences recited in Claim 1.

Moreover, Applicants find no teaching or suggestion in the references, individually or combined, of the using the methods of Ausubel et al. in combination with a nucleic acid comprising a sequence as recited in Claim 1. More particularly, Applicants find no teaching or suggestion in the references, individually or combined, of a vector which comprises at least one nucleic acid of Claim 1, as recited in Claim 2; a host cell which contains a nucleic acid of Claim 1, as recited in Claim 4; a nucleic acid of Claim 1(c) which comprises a sequence that hybridizes with a sequence defined under (a) in 0.5 x SSC at 60°C or in 0.2 x SSC at 60°C, as recited in Claims 22 and 23, respectively; or of a process for preparing a polypeptide encoded by a nucleic acid of Claim 1 comprising culturing a host cell containing a nucleic acid of Claim 1 or a vector comprising at least one nucleic acid of Claim 1 under conditions which ensure expression of the nucleic acid, and isolating the polypeptide from the cell or the culture medium, as recited in Claim 10.

Ausubel et al. may suggest it is obvious to try the methods taught by Ausubel et al. in order to introduce a nucleic acid into cells, however, obvious to try is not to be equated with obviousness under 35 U.S.C. §103. *Gillette Co. v. S. C. Johnson & Sons, Inc.*, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990). The mere fact the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. *In re Gordon* 221 USPQ 1125, 1127 (Fed. Cir. 1984).

For the reasons set forth above, Shulte et al. is not a proper reference, and Claim 2-7 and 24-31 are not rendered obvious by any combination of Celniker et al., Liao et al., or Vogel et al. and Ausubel et al., whereby the rejection of Claim 2-7 and 24-31 under 35 U.S.C. § 103 based on any of Schulte, Celniker, Liao et al., or Vogel et al. in view of Ausubel et al. should be reversed.

For the reason set forth above, Applicants submit that the claims herein are supported by an enabling description, definite, and neither anticipated nor rendered obvious by the cited references and combination of references. The Examiner is therefore requested to withdrawn the rejection to the claims and to allow the application to pass to issue.

Respectfully submitted,

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